Scope and Status of Schiff base ligand and its Metal Complexes

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Abstract

Schiff base ligands are very important class of ligands. Their metal complexes have been of great interest for many years. Schiff bases are common ligands but they are extremely different in properties then other ligands in coordination chemistry. Due to extraordinary behavior of Schiff base, transition metals are attracted readily to from complexes with Schiff base. A simple procedure of condensation of amine and aldehyde or ketone produces a vast variety of Schiff base ligands. The chelation effect of Schiff base ligands make them more prominent to complexation. Schiff base ligands can be substituted with variety of electron-donating or electron-withdrawing groups and create different chemical environment which contributes effectively in preparation of transition metal complexes.

Schiff base ligands and their metal complexes have shown fabulous applications in many fields. Schiff base metal complexes serve as catalysts in many reactions and also using as chemical sensors. Research shows activities of Schiff base complexes like antioxidant, radical scavenging, cytotoxicity, antitumor, anticancer, antimalarial, antibacterial, antiviral, antifungal, antipyretic, antileprosy, anti-inflammatory and anti-HIV. These complexes gave adequate path for human welfare by developing DNA-binding, DNA cleavage and drug-DNA interaction. Biological activities of Schiff base complexes are of main concern nowadays. In fact, a huge area of bio-inorganic is occupied by Schiff base and their metal complexes.

Keywords

Schiff Base, Transition Metal Complexes, Biological Activities.

Introduction

Schiff bases are important class of compounds due to their flexibility, structural similarities with natural biological substances and also due to the presence of imine moiety (-N=CH-) which is potential in elucidating the mechanism of transformation and resamination reaction in biological system [Valarmathy et al., 2013].

A Schiff base is a compound with general structure R2C=NR' (R' '" H). Schiff bases can be synthesized by condensation of primary amines with carbonyl compounds (aldehydes and ketones). A German chemist "Hugo Schiff" who was a nobel prize winner given Schiff base firstly. These compounds are also known as anils, imines or azomethines [Hossain et al., 2017]. The electrophilic carbon atoms of aldehydes or ketones can be targets of nucleophilic attack by amines. The end result of this reaction is a compound in which C=O double bond is replaced by a C=N double bond.

Coordination of metal ions by different ligands changes the reduction-oxidation potentials of a reaction, making it easier or sometimes more difficult to occur. The mechanism of reaction can involve binding to a metal in vivo or the metal complex may act as a vehicle for the activation of ligands [Goel et al., 2016]. Metal complexes play an essential role in agriculture, pharmaceutical and industrial chemistry [Kumar et al., 2009].

Schiff bases and their metal complexes are used as catalysts in various biological systems, polymers and dyes. Their use in birth control, food package also in consideration [Kumar et al., 2009]. Rhodanine derivatives are known to possess biological activities such as anticonvulsant, antibacterial, antiviral and antidiabetic [Elzahany et al., 2008]. Schiff base complexes show a broad range of biological activities for antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral and antipyretic properties [Abu-Dief et al., 2015].

During past two decades, the field of Schiff bases and their metal complexes is more active because it contains nitrogen and other donors [Tai et al., 2003]. Schiff bases provide potential sites for biochemically active compounds. Various transition and inner-transition metal complexes with bi, tri and tetradentate ligands. Schiff bases containing nitrogen, oxygen or sulphur donor atoms play an important role in biological systems [Alias et al., 2014]. These complexes showed activity such as antiviral, antibacterial, antifungal, antiphrastic, antitumor, anticancer and anti-HIV [Hossain et al., 2017].

Schiff base metal complexes serve as model for biologically important species. The metal complexes showed more potential to react against bacterial species and microbes as compared to parent ligands [Mohamed Gehad G., 2006]. The existance of metal ions bonded to biologically active compounds enhance their activities.

Sometimes, preparation of Schiff base ligands is difficult to take place. It leads to adopt a alternative way, such as template condensation. The template condensation methods lie at the heart of macrocyclic chemistry. Transition metals played a role as templating agent [El-Boraey and El-Gammal., 2018]. The transition elements V, Cr, Mn, Fe, Co, Ni, Cu and Zn are present in trace quantities but serving as a backbone in a living system at the molecular level. These transtion metals are known to form Schiff base complexes.

Schiff base (imine)

Schiff bases are common ligands in coordination chemistry. Schiff bases are generally bidentate, tridentate, tetradentate or polydentate ligands. This classification is basically depends upon the number of donor atoms present, such as Nitrogen (N), Oxygen (O) and Sulphur (S). These Schiff base ligands are expanded enormously to combine with metal ion and produce very stable complexes. Schiff bases have a wide variety of applications in different areas, such as biological chemistry, organic and inorganic chemistry [Mumtaz et al., 2016].

Chelation

The chelation effect of Schiff base ligands make them more prominent to complexation. Schiff base and their metal(II) complexes have been attracted due to their preparative accessibility, structural variability and electronic properties. Transition metals are known to form Schiff base complexes and Schiff base have been used as chelating ligands in coordination chemistry. Their flexibility by showing more than one oxidation state supported many synthesis.

As the chelation property of Schiff base plays a vital role in the system. The biological activities of the metal chelates against bacteria *Staphylococcus aureus*, *Bacillus subtilis*, *Salmonella typhi* and fungi reported [Raman N. et al., 2007]. For the last few years, chelation behaviour of Schiff base towards some transition elements has been reported. Basically, chelating ligands and mode of chelation has been used for determining the elements. A neutral chelating ligands on the complexation with iron to determine it in different types of natural water by using recovery test [Khalil et al., 2012].

DNA Binding and DNA Cleavage

Literature overview shows that Schiff base metal complexes are also known for DNA binding ability, DNA cleavage activity and drug-DNA interaction. DNA is made up of molecules called nucleotides. Nucleotides contain a nitrogenous base, due to which they act as nucleophile whereas the metal ions beared charge and act as electrophile. There are wide series of complexes showing activity with DNA. DNA binding and cleavage have been shown by ligand and its metal complexes, investigated also by using pUC18DNA gel elctrophoresis as well as drug-DNA interaction reported [Aziz et al., 2017; Shabbir et al., 2017].

Similarly, Schiff bases (2-benzo[d]thiazol-6-ylimino)methyl)-4,6-dichlorophenol) and (1-benzo[d]thiazol-6-ylimino)methyl)-6-bromo-4-chlorophenol) have been used to derive Co(II), Ni(II) and Cu(II) metal complexes. The interaction of these metal complexes with Calf thymus-DNA has been shown. Cu(II) complexes possessed DNA cleavage more actively with pBR322DNA than Co(II) and Ni(II) complexes [Daravath et al., 2017]. A Schiff base thiosemicarbazone ligand derived from 4-phenylthiosemicarbazide and sodium salicylaldehyde-5-sulfonate (NaSalSO3). During DNA fragmentation assay studies Ni(II) complexes has been found to induce apoptosis in the K562 cell line [Hosseini-Yazdi et al., 2017]. Ferocene-based Schiff base Co(II) complexes are also known for DNA protection against hydroxyl free ligands and DNA-Drug interaction [Shabbir et al., 2017].

Sensors

Metal complexes of Schiff base ligands are shown in the application of sensor also. Basically, chemical sensor is a device that transforms chemical information in an analytically useful signal. They can have application in many field like environment pollution, medicine, home safety and others. Naphthalene derivatives are known for their potential photosensitive biological units and photo induced electron transfer sensors. Schiff bases are also reported as fluorescent chemo sensor [Banaei A. Et al., 2016].

Catalysts

Schiff base and their metal complexes show a wide variety of catalytic reactions. Fe(II) complexes play an important role in developing catalysis studies [Babu et al., 2017]. They also catalyse reactions on oxygenation, hydrolysis, electro-reduction and decomposition [Kumar et al., 2009]. Co(II) complexes possessed ability of catalysis in living system. Copper is also embedded in enzymes in biological system which opens the door of catalytic reaction [Borthakur et al., 2015].

Schiff bases are used as catalysts in the field of medicine and industry. Metal complexes of Schiff base ligands have been used as precursors in the preparation of nanostructures of the respective metal oxides [Hasan et al., 2016]. Many literature studies show the application of Schiff bases and their complexes in homogenous and hetrogenous catalysis [Abu-Dief et al., 2015]. Their applications as catalyst have been reported in polymerization reaction, aldol reaction, Henry reaction and in Diels Alder reaction [Islam et al., 2018].

Antibacterial and Antimicrobial

A series of metal complexes using Schiff base ligands showed activity against Gram positive and Gram negative bacteria and determined MIC value [Guguloth, 2015]. This bioactivity was substained with SEM study [Pd (L)(Cl)] possess bactericidal as well as bacteriostatic activity [Bandyopadhyay et al., 2015]. Semisynthetic pencillin type antibiotic also affect growth of Gram positive and Gram negative bacteria by preventing cell wall formation [Chaudhary and Mishra, 2017].

The cup plate method and MIC are used for screening the antibacterial activity by liquid dilution method [Babu et al., 2017]. Two azo group containing Schiff base ligands and their complexes are synthesized which also showed antimicrobial activity [Orojloo et al., 2017]. The compound [CuLphen] showed antimicrobial activity and Cu(II) complexes with semicarbazones and thiosemicarbazones are also reported [Osowole et al., 2012; Goel et al., 2016].

Antioxidant and Radical Scavenging

The Schiff bases and their metal complexes were reported for their antioxidant and radical scavenging [Goel et al., 2016]. Antioxidant activity of the compounds was evaluated and the thiosemicarbazone ligand indicated the radical scavenging relative to Ni(II), Cu(II) and Zn(II) complexes and L-ascorbic acid as a water soluble standard [Hosseini-Yazdi et al., 2017].

Cytotoxicity and Antitumor Activities

Schiff bases prepared using biopolymer chitosan which contributed in study of cytotoxicity tests when combined with metal ions. Cytotoxicity tests were performed using MTT assay with HeLa cells or other cells. Schiff base metal complexes have been shown high toxicity as compared to free Schiff base ligands [Orojloo et al., 2017]. The biological studies of Copper(II) complexes with bidentate Schiff bases revealed cytotoxicity and antitumor nature [Shabbir et al., 2017].

Miscellaneous Applications

Schiff base ligands and their complexes are attributed to many other application, like pigment and dyes industries, polymer stablizer [Hossain et al., 2018], to extract specific metals and also in biological system photosynthesis, dioxygen transport [El-Boraly and EL Gammal, 2018]. Amino acids such as Methionine which are used in biosynthesis of proteins also developed stable Schiff base ligands.

Many Schiff base derivatives are also known which contain a pyrimidine unit starting with chalcones. Chalcones on further reaction produced oxopyrimidines and thioxopyrimidines [Tomma

et al., 2014]. Likewise, pyrazol derivatives also occupied a unique place and used extensively in medicinal chemistry [Singh et al., 2016].

Electrochemical study revealed significant dependence of redox properties on Schiff base ligand skeleton [Pogany et al., 2017]. The Sulfa drug, Sulfamerazine and Bipyridine produced stable novel mixed-ligand complexes of Cu(II), Ni(II) and Co(II) [Maurya et al., 2006]. The Sulpha drug derivatives widely used in clinical medicine as pharmacological agents. Dapsone showed antileprosy activity [Menaga and Rama., 2018].

The Schiff base ligands which are di-, tri-, tetra-, penta- and polydentrate combined with metal ions to produce very stable metal complexes. Literature data revealed that Schiff base ligands and their metal complexes exhibit excellent activities.

Nowadays, Schiff bases and their metal complexes are centre of attraction in the field of research due to the following behaviour:

1. The chelation effect of Schiff base ligands make them more prominent to complexation. This property contributes effectively in preparation of transition metal complexes.
2. Schiff base ligands can be substituted with variety of electron-donating or electron withdrawing groups and create different chemical environment which again plays significant role in Schiff base metal complexes.
3. Synthesis of Schiff base ligand is not much complex, but it becomes difficult to reach the product in some reactions. In such cases, a ligand based template reactions prove as boon. Template reaction produces the desired product with same reactant and also increase the yield of ligand.
4. Endlessly, Schiff base ligands also fulfill the essential need for extraction of metal ions depending on their nature and structure.

Conclusion

This paper comprises precise approach to infinite scope and applications of Schiff base and their metal complexes. Due to extra ordinary behavior of Schiff base transition metals are very compatible to attach firmly with each other. In recent years, transition metal complexes are reported for their vast contribution in the area of medicine and pharmaceutical. So Schiff base and their metal complexes provide boundless opportunities for research.

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